Pyothorax and pulmonary lymphomatoid granulomatosis in a cat

Abstract

A 7-year-old female neutered British Short Hair cat was presented for further investigation and treatment of pleural effusion due to a possible pyothorax.

Cytology and culture of the fluid identified pyothorax and a large mass/consolidated right caudal lung lobe was found on x-ray, ultrasound and CT scan. Lung lobectomy was performed and a diagnosis of pulmonary lymphomatoid granulomatosis (PLG) was confirmed by histopathology and immunohistochemistry. Despite medical treatment the patient was euthanized due to progression of the disease and deterioration of her clinical signs.

This is the second case of PLG reported in a cat and the first case of PLG with concurrent pyothorax. PLG, despite being very rare, should be added to the list of differential diagnoses for pyothorax and solitary lung masses in cats.

Case history

A 7-year-old, female, neutered, British Short Hair cat was presented for further investigation of dyspnoea.

The cat had outdoor access, was regularly vaccinated and wormed, with no history of previous significant illness apart from occasional fighting with the neighbour's cat. She was presented to the referring veterinarian with a week of progressive increased respiratory effort. She was treated with subcutaneous cefovecin injection with no improvement. Thoracic radiography suggested a right sided pleural effusion. The fluid was drained and pyothorax was suspected. The cat was referred for further investigation and treatment.

On physical examination the patient was bright and alert with mild dyspnoea and tachypnoea (48 brpm), body temperature was mildly elevated 39.5^{o} C. On auscultation of the thorax, lung sounds were absent on the right side with normal sounds on the left. The remainder of the physical examination was unremarkable.

Haematology, biochemistry, FIV and FeLV snap tests®, thoracic radiography and thoracic, abdominal and cardiac ultrasound were performed. Biochemistry was unremarkable and FIV and FeLV testing was negative. Haematology showed mild left shift neutrophilia with toxic changes in some neutrophils (Dohle bodies).

Cardiac and abdominal ultrasound were unremarkable. Thoracic ultrasound revealed a moderate amount of hyperechoic, swirling pleural fluid, with the lung itself having a moderately homogeneous, soft tissue echotexture.(Fig.1). The thoracic radiographs were repeated after the drainage of 60 mls of pleural effusion. There was a large soft tissue opacity present in the right caudal thoracic cavity, which was displacing the cardiac silhouette to the left. There was no obviously aerated lung in the region.

The pleural fluid consisted of a high protein, neutrophil-rich exudate with intracellular cocci, consistent with pyothorax.

Unidentified anaerobic bacteria sensitive to metronidazole were cultured from the fluid.

The cat was hospitalised and pending culture and sensitivity results, was treated with potentiated amoxicillin, marbofloxacin and meloxicam. Metronidazole was added after the results of the culture of the pleural effusion, however this treatment resulted in no improvement.

A CT scan of the thorax with iohexol contrast medium was performed. There was marked enlargement of the right caudal and accessory lung lobes. In the central region of the these lobes, the normal pulmonary parenchyma was completely replaced by a more attenuating, homogeneous, contrast enhancing tissue, whereas the periphery was relatively more hypoattenuating and non-contrast enhancing (Compatible with atelectasis). (Fig .2). A moderate amount of pleural effusion was present, particularly in the right cranial hemithorax. Bronchoscopy demonstrated complete occlusion of the right caudal lobe bronchus with pale cream tissue discharging purulent material. This correlated with the CT findings. Grab biopsy and BAL were performed but neither proved diagnostic. Culture was negative, however the cat was on multiple antibiotics at this point.

Considering the high suspicion of a neoplastic process, the lack of visible involvement of other portions of the lungs and negative staging elsewhere in the body, a lung lobectomy for diagnostic and therapeutic purposes was performed. The right caudal and accessory lung lobes were resected via an intercostal surgical thoracotomy. The thorax was drained, flushed and a right sided thoracic drain was placed.

The patient recovered well, and the histopathology analysis of the consolidated lung showed unencapsulated, infiltrative and densely cellular round cell tumor associated with extensive areas of coagulative necrosis (Fig n.3). The neoplastic cells were arranged in sheets and cuffs surrounding and extending into the vascular walls ; and were supported by a scant collagenous stroma. The vast majority of the neoplastic cells are round, intermediate to large sized, with indistinct or moderately well-defined cell borders and a scant pale eosinophilic cytoplasm. The nuclei are round to ovoid, occasionally irregularly shaped, with a nuclear diameter equivalent to or greater than 1.5 erythrocytes, a finely stippled chromatin and one to three prominent nucleoli. The mitotic count was 52 mitoses per 10 high power fields (per 2,37 mm^2). Anisocytosis and anisokaryosis were moderate throughout the neoplastic cell population. Occasional multinucleated neoplastic cells with up to 4 nuclei randomly distributed were present. More than 95% of neoplastic cell population exhibited an intense cytoplasmic staining for CD20 (B cell origin). Approximately 10-30% of the neoplastic cells exhibited a cytoplasmic staining for CD79α or a nuclear staining for Pax5 (B cell markers). Additionally, small aggregates of CD3-positive mature lymphocytes (T cell origin) and plasma cells, together with a few neutrophils and macrophages exhibiting a cytoplasmic staining for MAC387, were scattered within the tumour (Fig n.4). Histologic and immunohistophenotypic profile was suggestive of a B cell angiocentric and angiodestructive lymphoma, with the presence of a reactive population of T lymphocytes and plasma cells, also called pulmonary lymphomatoid granulomatosis (PLG)and the histopathology analysis of the consolidated lung showed an angiocentric and angiodestructive lymphoprolipherative process associated with extensive areas of coagulative necrosis (Fign.3). The neoplastic cell population was primarily composed of CD20-positive lymphoid cells (B cell origin). Approximately 10-30% of the neoplastic cells exhibited a cytoplasmic staining for CD79α or a nuclear staining for Pax5 (B cell markers). Additionally, small aggregates of CD3-positive mature lymphocytes (T cell origin) and plasma cells, together with a few neutrophils and macrophages exhibiting a cytoplasmic staining for MAC387, were scattered within the tumour (Fign.4). Histologic and immunohistophenotypic profile was suggestive of a B cell angiocentric lymphoma, with the presence of a reactive

population of T lymphocytes and plasma cells, also called pulmonary lymphomatoid granulomatosis (PLG). Culture of the lung was negative.

The patient started to deteriorate a few days following surgery and an increasing amount of pleural effusion was drained each day. Soon after diagnosis the cat was treated with high dose subcutaneous dexamethasone (0.3mg/kg) and a moderate clinical improvement was noticed the following day. She was then started on vincristine 0.7 mg/m^2, however the dyspnoea and tachypnoea worsened again. Thoracic ultrasonography demonstrated progression of the disease due to a moderate amount of pleural effusion in the left hemithorax, with consolidation of the lung lobes and rounding of their edges. Pleural fluid analysis was repeated and showed a neoplastic effusion with large amount of large lymphocytes. Based on the disease progression and the clinical deterioration despite oxygen treatment, the patient was euthanized. Post mortem examination was not performed.

Discussion

PLG is a very rare disease of dogs and humans(1,2,3). PLG in people, has been seldom associated to Epstein Barr virus infection, but in many cases as in veterinary medicine the aetiology remain unknown(4). A single case has been reported in a cat(5). PLG has not previously been associated with pyothorax.. A potential pathogenesis in this case is extension of infection from a secondarily infected necrotic area within the PLG. Bacteria were not found on the lung culture or on histopathology, however this could be due to the multiple combinations of antibiotics the patient had been treated with. The multiple areas of necrosis present within the affected lungs could be due to the angiocentric infiltration of the neoplastic cells causing reduced blood flow and formation of foci of ischaemic coagulative necrosis. Less likely causes of the pyothorax include a haematogenous bacterial infection from an undetected source or a penetrating injury that could have been inflicted during a cat fight, with the PLG and pyothorax being unrelated in these scenarios. These hypothesis are less likely, in particular considering the CT findings, which indicated that the pleural effusion was worse on the right, where the PLE was located.

During ultrasound and later the CT scan, FNA and/or tru-cut® lung biopsy were discussed but were not undertaken. Considering the lack of visible extension of the disease elsewhere in the thorax and abdomen, performing a lobectomy was considered more beneficial in terms of diagnostic and therapeutic benefits. Lobectomy of the affected lung would obtain a larger and more representative sample of the disease, avoiding the risk of sampling diffuse areas of necrosis instead of the neoplasia, and would avoid the possible risks of FNA/tru-cut related procedure complications in particular pneumothorax and haemothorax; the risks of sampling a necrotic area of the lung with consequent extension of the necrotic/infectious process to the thorax were also discussed, however pyothorax was already present and so this potential complication was considered less important. Lobectomy could also have had a therapeutic benefit if the lung consolidation was due to a solitary lung carcinoma.

A diagnosis of PLG is difficult to achieve by cytology only, because the typical pathognomonic angiocentric architecture can be seen only on histopathology analysis(5). A broader cytological diagnosis of lymphoid lymphoproliferative disease would also have been difficult in our case due to the presence of a mixed population of cell infiltrate seen on histopathology. However, a suspected diagnosis of lymphoid neoplasia (most of the infiltrate was represented by large

lymphocytes) may have been possible, if a diagnostic sample had been obtained on FNA. In this scenario, the treatment could have been started immediately, avoiding surgery and the longer time taken for the histopathological diagnosis.

The PLG in dogs has been described to have a various response to prednisolone and different chemotherapy treatments, with high response rate and long-term survival time often reported (6,7). Response to chemotherapy and prognosis in cats are completely unknown and treatment was not attempted in the only case report found in the literature. In our case the patient did not respond to dexamethasone or vincristine and the disease progressed rapidly. The possibility that an earlier diagnosis and an earlier treatment with chemotherapy would have changed the outcome of this case is unlikely, due to the lack of significant response to both dexamethasone and vincristine. However, an early treatment with possible different chemotherapies could have been more successful.

In this case there was no clinical benefit from resecting the affected lung lobe, but it is possible that in the early stage of the disease this could have been more beneficial. In this case no extension of the disease to the abdominal or thoracic organs was seen on the thoracic CT scan and abdominal ultrasound examination, so the decision to remove the lung lobes was made for both diagnostic and therapeutic purpose. However, FNA samples of other organs like spleen and liver where not performed, and though unlikely, a generalised disease could not be ruled out completely.

This is the second report of PLG in cats, but the only case in which PLG has been diagnosed in combination with pyothorax which complicated the diagnosis and where medical and surgical treatment have been attempted. PLG could be a rare underlying cause of pyothorax and should be added to the literature for differential causes of pyothorax in cats.

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

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Fig 1:
Ultrasound image of the right caudal thoracic cavity. The right caudal lung lobe has a moderately homogeneous soft tissue echotexture.

Fig 2:
Post contrast CT of the thorax at the level of the 7th intercostal space. The right caudal lung lobe is markedly enlarged and filling the majority of the right caudal hemi-thorax. The periphery is hypoattenuating and non-contrast enhancing, however the central portion is mildly to moderately contrast enhancing. There is a moderate amount of pleural fluid visible on the ventral aspect of the right thoracic cavity (Arrow head). The heart is visible on the left (arrow), being displaced by the enlarged lung lobe.

Fig 3 Right caudal lung lobe, cat. Perivascular and intramural infiltrates of densely packed mononuclear cells. There is coagulative necrosis and oedema in the adjacent alveolar parenchyma. HE. Scale bar = 500 µm.

Figure 4 Atypical large lymphoid cells with small numbers of other lymphoid cells and histiocytes. Note multinucleated cell (arrow). HE. Scale bar = 30 µm.

Fig 5 Right caudal lung lobe, cat. Immunohistochemical panel including antibodies against CD20, CD79α, Pax5, CD3 and MAC387. IHC. Black insets: scale bar = 500 µm. Red inset: scale bar = 100 µm.